FORM PTO-1390 (REV 10-95) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. §371

ATTORNEY'S DOCKET NUMBER: MERCK 2293

U.S. APPLICATION NO. (If known, see 37 CFR §1.5): 09/889930

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/EP00/00569	26 JANUARY 2000	28 JANUARY 1999

TITLE OF INVENTION: LYOPHILISATES HAVING IMPROVED RECONSTITUTABILITY

APPLICANT(S) FOR DO/EO/US: KURZ, Thekla, et al.

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ■ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. §371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. §371.
3. ☐ This express request to begin national examination procedures (35 U.S.C. §371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. §371(b) and PCT Articles 22 and 39(1).
4. ■ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. ■ A copy of the International Application as filed (35 U.S.C. §371(c)(2))
   a. ☐ is transmitted herewith (required only if not transmitted by the International Bureau).
   b. ■ has been transmitted by the International Bureau.
   c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ■ A translation of the International Application into English (35 U.S.C. §371(c)(2)).
7. ■ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. §371(c)(3))
   a. ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☐ have been transmitted by the International Bureau.
   c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ■ have not been made and will not be made.
8. ☐ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. §371(c)(3)).
9. ☐ An oath or declaration of the inventor(s) (35 U.S.C. §371(c)(4)).
10. ☐ A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. §371(c)(5)).

Items 11. to 16. below concern document(s) or information included:

11. ☐ An Information Disclosure Statement under 37 C.F.R. §§1.97 and 1.98.
12. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 C.F.R. §§3.28 and 3.31 is included.
13. ■ A FIRST preliminary amendment.
    ☐ A SECOND or SUBSEQUENT preliminary amendment.
14. ☐ A substitute specification.
15. ☐ A change of power of attorney and/or address letter.
16. ☐ Other items or information:

JC17 Rec'd PCT/PTO 25 JUL 2001

U.S. APPLICATION NO. (if known, see 37 CFR §1.5)	INTERNATIONAL APPLICATION NO.	ATTORNEY'S DOCKET NUMBER
09/889930	PCT/EP00/00569	MERCK 2293

17. ☒ The following fees are submitted:

	CALCULATIONS PTO USE ONLY
BASIC NATIONAL FEE (37 CFR §1.492 (a) (1) - (5)):	
Search Report has been prepared by the EPO or JPO..... $860.00	
International preliminary examination fee paid to USPTO (37 CFR §1.482)..... $690.00	
No international preliminary examination fee paid to USPTO (37 CFR §1.482) but international search fee paid to USPTO (37 CFR §1.445(a)(2))..... $710.00	
Neither international preliminary examination fee (37 CFR §1.482) nor international search fee (37 CFR §1.445(a)(2)) paid to USPTO..... $1000.00	
International preliminary examination fee paid to USPTO (37 CFR §1.482) and all claims satisfied provisions of PCT Article 33(2)-(4)..... $100.00	
ENTER APPROPRIATE BASIC FEE AMOUNT =	$860.00
Surcharge of **$130.00** for furnishing the oath or declaration later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 C.F.R. §1.492(e)).	

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE	
Total claims	12 - 20 =	0	x $ 18.00	$0.00
Independent claims	5 - 3 =	2	x $ 80.00	$160.00
MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ $ 270.00	

TOTAL OF ABOVE CALCULATIONS =	$1,020.00
Reduction of 1/2 for filing by small entity, if applicable. A Verified Small Entity Statement must also be filed (Note 37 C.F.R. §§1.9, 1.27, 1.28).	
SUBTOTAL =	$1,020.00
Processing fee of **$130.00** for furnishing the English translation later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 C.F.R. §1.492(f)).	
TOTAL NATIONAL FEE =	$1,020.00
Fee for recording the enclosed assignment (37 C.F.R. §1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 C.F.R. §§3.28, 3.31). $40.00 per property.	
TOTAL FEES ENCLOSED =	$1,020.00
Amount to be refunded:	
charged:	

a. ■ A check in the amount of $1,020.00 to cover the above fees is enclosed.

b. ☐ Please charge my Deposit Account No. 13-3402 in the amount of $ _____ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. ■ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 13-3402. A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 C.F.R. §§1.494 or 1.495 has not been met, a petition to revive (37 C.F.R. §1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO: Customer Number 23,599

23599
PATENT TRADEMARK OFFICE

SIGNATURE

Anthony J. Zelano
NAME

27,969
REGISTRATION NUMBER

Filed: 25 JULY 2001

AJZ:kmo

IN THE UNITED STATES DESIGNATED/ELECTED OFFICE

International Application No.	:	PCT/EP00/00569
International Filing Date	:	26 JANUARY 2000
Priority Date(s) Claimed	:	28 JANUARY 1999
Applicant(s) (DO/EO/US)	:	KURZ, Thekla, et al.

Title: LYOPHILISATES WITH IMPROVED RECONSTITUTIBILITY

PRELIMINARY AMENDMENT

Commissioner for Patents
Washington, D.C. 20231

SIR:

Prior to calculating the national fee, and prior to examination in the National Phase of the above-identified International application, please amend as follows:

IN THE CLAIMS:

Please amend the claims as follows:

3. (Amended) Process according to Claim 1, characterized in that lyophilisates are obtained which can be reconstituted in a particle-free manner.

4. (Amended) Process according to Claim 1, characterized in that lyophilisates of the substance 2-methyl-5-methylsulfonyl-4-(1-pyrrolyl)benzoylguanidine methanesulfonate, N-[2-methyl-4,5-bis-(methylsulfonyl)benzoyl]guanidine hydrochloride or 4-isopropyl-3-methylsulfonylbenzoylguanidine methanesulfonate are prepared.

9. (Amended) Pharmaceutical preparation comprising at least one lyophilisate according to Claim 5.

Please add the following new claims 10-12:

--10. Pharmaceutical preparation comprising at least one lyophilisate according to Claim 6.

11. Pharmaceutical preparation comprising at least one lyophilisate according to Claim 7.

12. Pharmaceutical preparation comprising at least one lyophilisate according to Claim 8.--

REMARKS

The purpose of this Preliminary Amendment is to eliminate multiple dependent claims in order to avoid the additional fee. Applicants reserve the right to reintroduce claims to canceled combined subject matter.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached pages are captioned "Version With Markings to Show Changes Made".

Respectfully submitted,

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AJZ:jmm

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

Claims 3-4 and 9 have been amended as follows:

3. (Amended) Process according to Claim 1 ~~or 2~~, characterisized in that lyophilisates are obtained which can be reconstituted in a particle-free manner.

4. (Amended) Process according to ~~one of~~ Claims 1 ~~to 3~~, characterisized in that lyophilisates of the substance 2-methyl-5-methylsulfonyl-4-(1-pyrrolyl)benzoylguanidine methanesulfonate, N-[2-methyl-4,5-bis-(methylsulfonyl)benzoyl]guanidine hydrochloride or 4-isopropyl-3-methylsulfonylbenzoylguanidine methanesulfonate are prepared.

9. (Amended) Pharmaceutical preparation comprising at least one lyophilisate according to Claims ~~5-8~~.

Claims 10-12 have been newly added therefore no marked-up version is necessary.

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PCT

WELTORGANISATION FÜR GEISTIGES EIGENTUM
Internationales Büro

INTERNATIONALE ANMELDUNG VERÖFFENTLICHT NACH DEM VERTRAG ÜBER DIE INTERNATIONALE ZUSAMMENARBEIT AUF DEM GEBIET DES PATENTWESENS (PCT)

(51) Internationale Patentklassifikation 7 :
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(81) Bestimmungsstaaten: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO Patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), eurasisches Patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), europäisches Patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI Patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Veröffentlicht
Mit internationalem Recherchenbericht.
Vor Ablauf der für Änderungen der Ansprüche zugelassenen Frist; Veröffentlichung wird wiederholt falls Änderungen eintreffen.

(54) Title: LYOPHILISATES WITH IMPROVED RECONSTITUTIBILITY

(54) Bezeichnung: LYOPHILISATE MIT VERBESSERTER REKONSTITUIERBARKEIT

(57) Abstract

The present invention relates to lyophilisates with an improved dissolution rate and particle–free reconstitution. This is achieved by additionally heating the filled solutions to temperatures between 30° and 95° C and directly at the freezer dryer.

(57) Zusammenfassung

Die vorliegende Erfindung betrifft Lyophilisate mit verbesserter Lösungsgeschwindigkeit und partikelfreier Rekonstitution, was durch erneutes Erwärmen der bereits abgefüllten Lösungen direkt am Gefriertrockner auf 30° bis 95 °C erreicht wird.

Lyophilisates having improved reconstitutability

The present invention relates to lyophilisates having an improved dissolution rate and reconstitutability, and to a process for their preparation.

Lyophilisation, also known as freeze drying, is a long-known and widely used method for the preservation of certain substances under gentle conditions, such as, for example, heat-sensitive foods or especially medicaments. In this method, the substances are dried in the frozen state and can be restored into the original state particularly easily on addition of water or another solvent. In this method, the first step is generally freezing of the starting materials at temperatures down to –70°C. The water is subsequently removed from them by sublimation during the drying process, which is carried out in pressure-tight containers (lyophilisators) under a high vacuum, giving the freeze-dried substance.

Lyophilisation is employed in particular for the preservation of sensitive medicaments, since it is very important in the case of medicaments in particular that they do not change during storage, i.e. their structure does not change, rearrange or even decompose, which would mean a considerable impairment with respect to their efficacy.

Efforts are always made during freeze drying to incorporate the largest possible amount of active ingredient into the smallest possible volume. This results in concentrations in the vicinity of the saturation concentration of the active ingredient often being employed. This is necessary for the economic efficiency of the processes.

In theses cases, however, the lyophilisate often cannot be reconstituted in a particle-free manner after freeze drying has been carried out, meaning that parenteral administration is no longer possible. This is attributed to crystals which have formed due to cooling after the saturation solubility has been exceeded. The dissolution rate of crystals is significantly slower than that of molecules in amorphous form.

The object of the present invention was therefore to provide a process for the preparation of lyophilisates which have an improved dissolution rate and can be reconstituted in a particle-free manner, even if they are metered close to the saturation concentration.

Surprisingly, it has been found that warming of the solution already prepared for the freeze-drying process directly in the freeze drier and rapid cooling from this elevated temperature to the freezing temperature gives lyophilisates which achieve the desired advantageous properties.

The invention therefore relates to a process for the preparation of lyophilisates having an improved dissolution rate, characterised in that the corresponding solutions already drawn off for lyophilisation, which have, if necessary, previously been warmed in order to accelerate dissolution of the substance, filtered – optionally sterile-filtered – and drawn off, are re-warmed to from 30° to 95°C directly in the vials in the freeze drier, and the freezing phase is then carried out rapidly from this elevated temperature to the desired low freeze-drying temperature.

The feature "rapidly" in this connection means a period of from 10 minutes to 4 hours, preferably from 30 minutes to 2 hours, very particularly preferably from 30 minutes to 1 hour.
The desired freeze-drying temperature can be down to –70°C, a temperature of about –50°C preferably being used.

In the conventional freeze-drying process, the substance or active ingredient is warmed in order to accelerate dissolution. The dissolution is followed, in the case of sterile preparation, which is usual in the case of medicaments, by the steps of sterile filtration and drawing-off. These two steps may, depending on the size of the batch, take a few hours. In the process, the solutions automatically cool to room temperature. The freeze drier is thus then charged at room temperature, and the freezing phase is then carried out as quickly as possible from room temperature to about –50°C. The drying phase in the freeze drier then commences.

In the process according to the invention, the dissolution, filtration or sterile filtration and the drawing-off are carried out analogously to the known process. Then, however, the freeze drier is charged with the corresponding prepared vials at room temperature, and these vials are re-warmed to 30° – 95°C in the apparatus. The freezing phase is started from this elevated temperature and brought to the desired freezing temperature as quickly as possible. The drying phase is then carried out in the usual manner.

Due to the re-warming of the solutions, the saturation solubility is significantly increased, which is attributable to the reduction in the size of the water clusters. The increased solubility thus results in improved hydration. In the case of rapid cooling, firstly the water

molecules lack the time to form relatively large clusters, and secondly the active ingredient molecules lack the time to arrange themselves into crystal nuclei. The resultant product is accordingly amorphous and can be reconstituted in a particle-free manner.

The warming of the solutions takes place to temperatures of from 30° to 95°C, temperatures in the range from 30° to 70°C preferably being selected.

The process according to the invention thus enables significantly higher concentrations to be introduced into a volume. The drying time is thus reduced and the economic efficiency of the process is increased.

The lyophilisates prepared in this way exhibit an improved dissolution rate and can be reconstituted in a particle-free manner although they can be metered close to the saturation concentration.

The invention also relates to the preparation of lyophilisates of the substance 2-methyl-5-methylsulfonyl-4-(1-pyrrolyl)benzoylguanidine methanesulfonate by the process described here (see Example 1). This substance (EMD 96785), which is known, for example, from DE 4430861, is an NHE inhibitor which blocks the Na^+/H^+ ion pump in the myocardial cells. This prevents overacidification of the cells in the case of an infarction, which results in the death of myocardial tissue.

The invention also relates to the preparation of lyophilisates of the substance N-[2-methyl-4,5-bis(methylsulfonyl)benzoylguanidine hydrochloride by the process described here (see Example 2).

This substance (EMD 87580), which is known, for example, from EP 0 758 644 A1, is likewise an NHE inhibitor which blocks the Na^+/H^+ ion pump in the myocardial cells. This prevents overacidification of the cells during an infarction, which results in death of myocardial tissue.

The invention also relates to the preparation of lyophilisates of the substance 4-isopropyl-3-methylsulfonylbenzoylguanidine methanesulfonate by the process described here.

This substance (cariporide), which is known, for example, from EP 589 336, in likewise an NHE inhibitor.

The invention furthermore relates to pharmaceutical preparations comprising at least one lyophilisate according to the invention.
The pharmaceutical preparations can be used as medicaments in human or veterinary medicine. Suitable excipients are organic or inorganic substances which are suitable for enteral (for example oral), parenteral or topical administration and do not react with the lyophilisates, for example water, vegetable oils, benzyl alcohols, alkylene glycols, polyethylene glycols, glycerol triacetate, gelatin, carbohydrates, such as lactose or starch, magnesium stearate, talc or Vaseline. Suitable for oral administration are, in particular, tablets, pills, coated tablets, capsules, powders, granules, syrups, juices or drops, suitable for rectal administration are suppositories, suitable for parenteral administration are solutions, preferably oil-based or aqueous solutions, furthermore suspensions, emulsions or implants, and suitable for topical application are ointments, creams or powders. The preparations indicated may have been sterilised and/or comprise assistants, such as lubricants, preservatives, stabilisers and/or wetting agents, emulsifiers, salts for modifying the osmotic pressure, buffer

substances, colorants, flavours and/or a plurality of further active ingredients, for example one or more vitamins.
The preparations preferably comprise the lyophilisates, for example, for the preparation of injection preparations.

Even without further details, it is assumed that a person skilled in the art can utilise the above description in the broadest scope. The preferred embodiments are therefore merely to be regarded as descriptive disclosure, but in no way as a disclosure which is limiting in any way.
The complete disclosure content of all applications and publications mentioned above and below are incorporated into this application by way of reference.

Example 1

a)

100 mg of 2-methyl-5-methylsulfonyl-4-(1-pyrrolyl)benzoylguanidine methanesulfonate (an NHE inhibitor) are dissolved in 20 ml of water by warming to 40°C in order to accelerate the dissolution. The solution is subsequently sterile-filtered and drawn off into vials suitable for freeze drying. In the process, the solution cools to room temperature. The freeze drier is charged with the vials at room temperature, and these vials are subsequently re-warmed to about 50°C. The freezing is then carried out from +50°C to –50°C within 1 hour. The drying phase then proceeds in the conventional manner.

The resultant lyophilisates are amorphous and can be reconstituted in a particle-free manner.

b) Comparative Example

100 mg of 2-methyl-5-methylsulfonyl-4-(1-pyrrolyl)benzoylguanidine methanesulfonate are again dissolved in 20 ml of water with warming to 40°C. The solution is sterile-filtered and drawn off, during which the solution cools to room temperature.
The vials are then cooled from room temperature to –50°C over the course of 1 hour in the freeze drier and frozen.

In this conventional process, crystal formation occurs even during the lyophilisation, which results in the lyophilisates not dissolving completely during reconstitution. In order to obtain a lyophilisate comparable to a), the concentration here had to be reduced to 50 mg / 20 ml.

However, this means that a higher concentration of the active ingredient can be selected in the process according to the invention and nevertheless lyophilisates having an improved dissolution rate are obtained.

Example 2:

100 mg of N-[2-methyl-4,5-bis(methylsulfonyl)]benzoylguanidine hydrochloride are dissolved in 10 ml of water by warming to 40°C. The solution is subsequently sterile-filtered and drawn off into vials or ampoules suitable for freeze drying. The solution cools to room temperature in the process.

The freeze drier is cooled down to –59°C. The vials filled with the solution are warmed to +40°C in a drying cabinet and subsequently introduced into the freeze drier, which has already been cooled down to –50°C. The solution is frozen as quickly as possible. The drying phase is then carried out in the conventional manner.

Warming of the vials in the freeze drier followed by cooling (as described in Example 1) is likewise possible.

09/889930
JC17 Rec'd PCT/PTO 25 JUL 2001

Patent Claims

1. A process for the preparation of lyophilisates having an improved dissolution rate, characterised in that the corresponding solutions already drawn off for lyophilisation which have, if necessary, previously been warmed in order to accelerate dissolution of the substance, filtered – optionally sterile-filtered – and drawn off, are re-warmed to from 30° to 90°C directly in the vials in the freeze drier, and the freezing phase is then carried out rapidly from this elevated temperature to the desired low freeze-drying temperature.

2. Process according to Claim 1, characterised in that the vials containing the solutions are warmed to from 30° to 60°C in the freeze drier.

3. Process according to Claim 1 or 2, characterised in that lyophilisates are obtained which can be reconstituted in a particle-free manner.

4. Process according to one of Claims 1 to 3, characterised in that lyophilisates of the substance 2-methyl-5-methylsulfonyl-4-(1-pyrrolyl)benzoylguanidine methanesulfonate, N-[2-methyl-4,5-bis-(methylsulfonyl)benzoyl]guanidine hydrochloride or 4-isopropyl-3-methylsulfonylbenzoylguanidine methanesulfonate are prepared.

5. Lyophilisates having an improved dissolution rate, characterised in that, in the preparation of the lyophilisates, the corresponding solutions already drawn off for lyophilisation, which have, if

necessary, previously been warmed in order to accelerate dissolution of the substance, filtered or sterile-filtered and drawn off, are re-warmed to from 30° to 95°C directly in the vials in the freeze drier, and the freezing phase is then carried out rapidly from this elevated temperature to the desired low freeze-drying temperature.

6. Lyophilisates of the substance 2-methyl-5-methylsulfonyl-4-(1-pyrrolyl)benzoylguanidine methanesulfonate having improved reconstitutability, characterised in that, in the preparation of the lyophilisates, the corresponding solutions already drawn off for lyophilisation, which have, if necessary, previously been warmed in order to accelerate dissolution of the substance, filtered or sterile-filtered and drawn off, are re-warmed to from 30° to 95°C directly in the vials in the freeze drier, and the freezing phase is then carried out rapidly from this elevated temperature to the desired low freeze-drying temperature.

7. Lyophilisates of the substance N-[2-methyl-4,5-bis(methylsulfonyl)-benzoyl]guanidine hydrochloride having improved reconstitutability, characterised in that, in the preparation of the lyophilisates, the corresponding solutions already drawn off for lyophilisation, which have, if necessary, previously been warmed in order to accelerate dissolution of the substance, filtered or sterile-filtered and drawn off, are re-warmed to from 30° to 95°C directly in the vials in the freeze drier, and the freezing phase is then carried out rapidly from this elevated temperature to the desired low freeze-drying temperature.

8. Lyophilisates of the substance 4-isopropyl-3-methylsulfonyl-benzoylguanidine methanesulfonate having improved reconstitut-

ability, characterised in that, in the preparation of the lyophilisates, the corresponding solutions already drawn off for lyophilisation, which have, if necessary, previously been warmed in order to accelerate dissolution of the substance, filtered or sterile-filtered and drawn off, are re-warmed to from 30° to 95°C directly in the vials in the freeze drier, and the freezing phase is then carried out rapidly from this elevated temperature to the desired low freeze-drying temperature.

9. Pharmaceutical preparation comprising at least one lyophilisate according to Claims 5-8.

Abstract

The present invention relates to lyophilisates having an improved dissolution rate which can be reconstituted in a particle-free manner, which is achieved by re-warming the solutions already drawn off to from 30° to 95°C directly in the freeze drier.

Docket No.
Merck 2293

Declaration and Power of Attorney For Patent Application
English Language Declaration

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name,

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled

LYOPHILISATES HAVING IMPROVED RECONSTITUTABILITY

the specification of which

(check one)

☐ is attached hereto.
☒ was filed on 26.01.99 as United States Application No. or PCT International Application Number PCT/EP00/00569
and was amended on _____ (if applicable)

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose to the United States Patent and Trademark Office all information known to me to be material to patentability as defined in Title 37, Code of Federal Regulations, Section 1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, Section 119(a)-(d) or Section 365(b) of any foreign application(s) for patent or inventor's certificate, or Section 365(a) of any PCT International application which designated at least one country other than the United States, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate or PCT International application having a filing date before that of the application on which priority is claimed.

Prior Foreign Application(s)			Priority Not Claimed
199 03 275.0 (Number)	Germany (Country)	28. January 1999 (Day/Month/Year Filed)	☐
(Number)	(Country)	(Day/Month/Year Filed)	☐
(Number)	(Country)	(Day/Month/Year Filed)	☐

I hereby claim the benefit under 35 U.S.C. Section 119(e) of any United States provisional application(s) listed below:

(Application Serial No.)	(Filing Date)
(Application Serial No.)	(Filing Date)
(Application Serial No.)	(Filing Date)

I hereby claim the benefit under 35 U.S.C. Section 120 of any United States application(s), or Section 365(c) of any PCT International application designating the United States, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States of PCT International application in the manner provided by the first paragraph of 35 U.S.C. Section 112. I acknowledge the duty to disclose to the United States Patent and Trademark Office all information known to me to be material to patentability as defined in Title 37, C.F.R., Section 1.56 which became available between the filing date of the prior application and the national or PCT International filing date of this application:

(Application Serial No.)	(Filing Date)	(Status) (patented, pending, abandoned)
(Application Serial No.)	(Filing Date)	(Status) (patented, pending, abandoned)
(Application Serial No.)	(Filing Date)	(Status) (patented, pending, abandoned)

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

POWER OF ATTORNEY: As a named inventor, I hereby appoint

I. William Millen (Reg. No. 19,544)
John L. White (Reg. No. 17,746)
Anthony J. Zelano (Reg. No. 27,969)
Alan E.J. Branigan (Reg. No. 20,565)
John R. Moses (Reg. No. 24,983)
Harry B. Shubin (Reg. No. 32,004)
Brion P. Heaney (Reg. No. 32,542)
Richard J. Traverso (Reg. No. 30,595)
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